



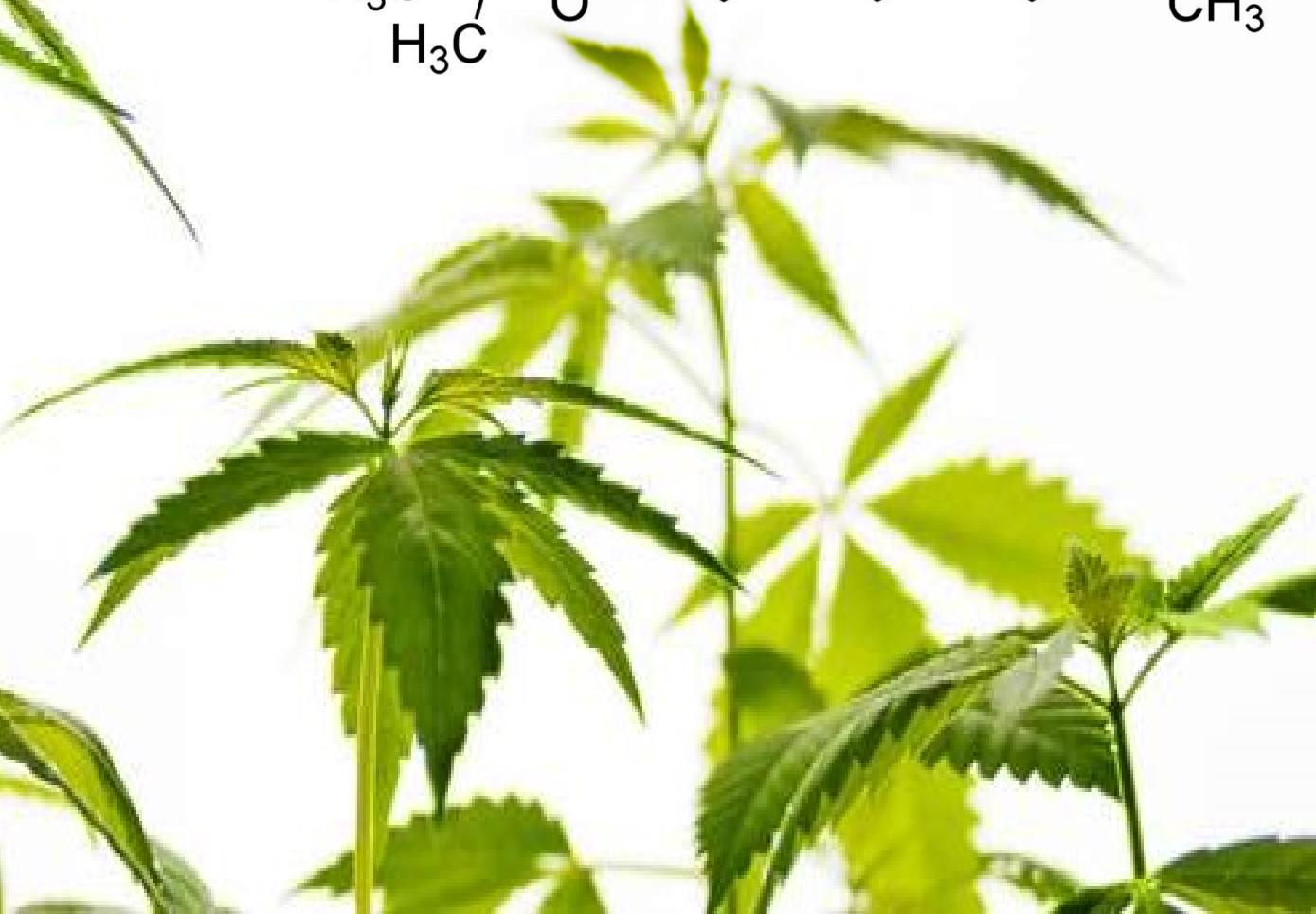
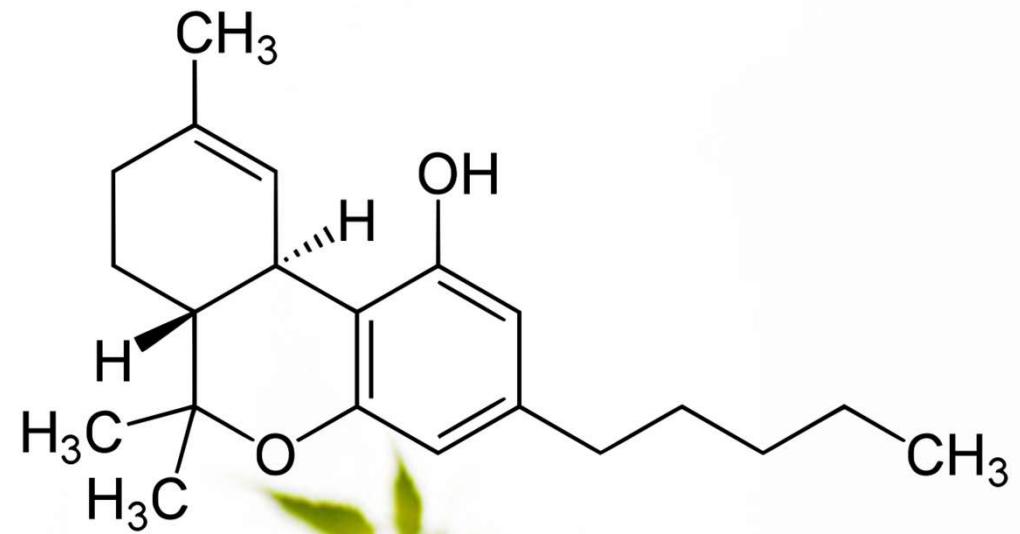
Was ist neu in der Kardiologie?

Klinik III für Innere Medizin
Herzzentrum der Universität zu Köln
12. Januar 2019

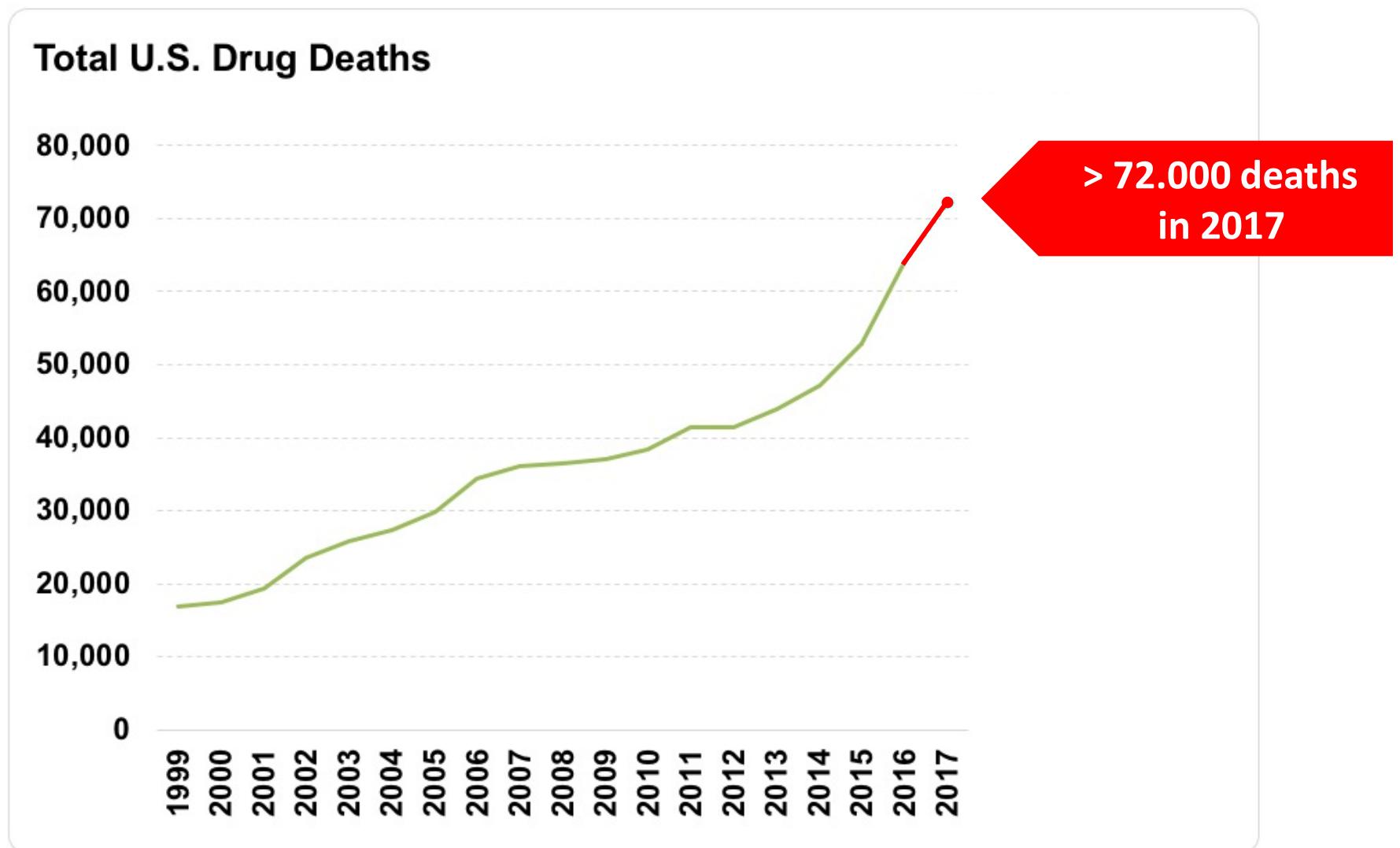


Kardiale Effekte moderner Lifestyle-Drogen

Stephan Rosenkranz
Klinik III für Innere Medizin
Zentrum für Molekulare Medizin Köln (ZMMK)
Cologne Cardiovascular Research Center (CCRC)
Herzzentrum der Universität zu Köln
stephan.rosenkranz@uk-koeln.de

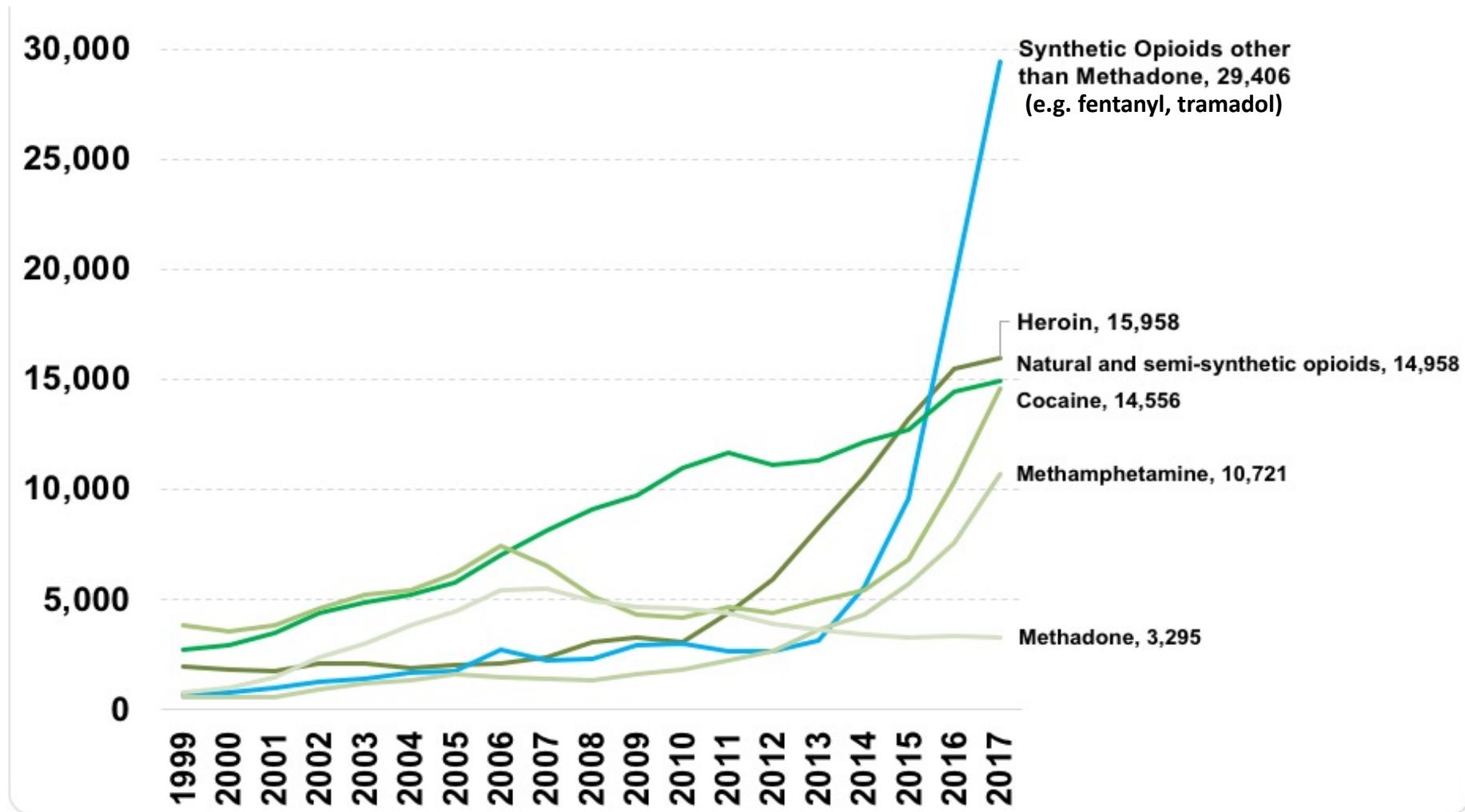


Drug Overdose Deaths: United States, 1999-2017



Source: Data Overview – drug overdose. CDC Injury Center, Centers for Disease Control and Prevention

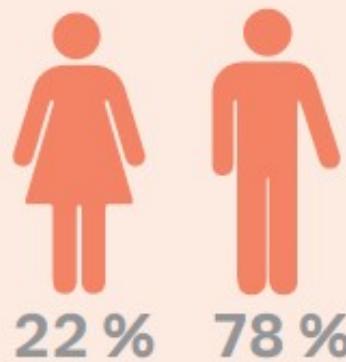
Drugs Involved in U.S. Overdose Deaths, 1999-2017



Source: Data Overview – drug overdose. CDC Injury Center, Centers for Disease Control and Prevention

Europäischer Drogenbericht 2018

Merkmale



Durchschnittsalter
der Verstorbenen

38

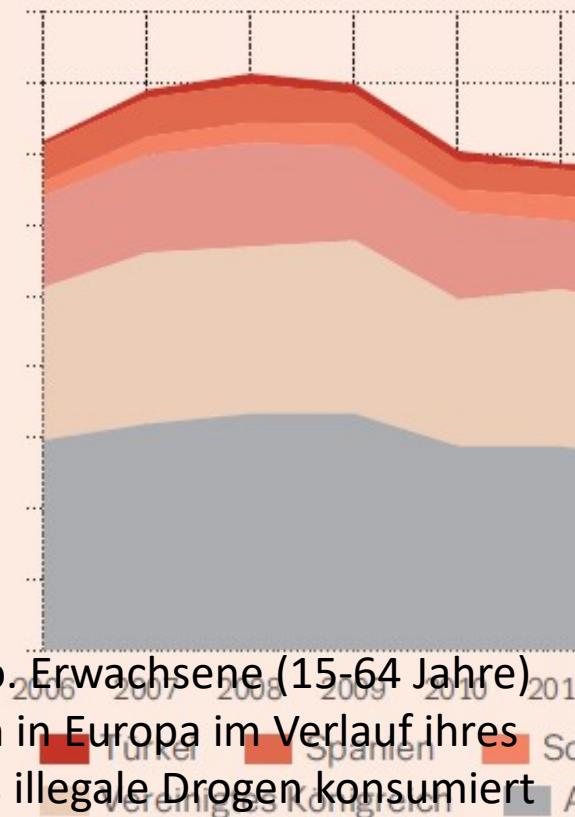
Todesfälle
im Zusammenhang
mit Opioiden



Alter der Verstorbenen



Trends in Bezug auf Todesfälle



,3 Millionen Menschen in Behandlung wegen des Konsums illegaler Drogen

Source: European Drug Report – European Union , EMCDDA

Europäischer Drogenbericht 2018

Cannabis



Erwachsene
(15-64)

Konsum:
Letzte 12 Monate
23,5 Millionen Lebenszeit
87,7 Millionen



Junge Erwachsene
(15-34)

Letzte 12 Monate
17,1 Millionen



Höchste 22,1 %
Niedrigste 3,3 %
Nationale Schätzungen
des Konsums in den letzten
zweihundert Monaten

Kokain



Erwachsene
(15-64)

Konsum:
Letzte 12 Monate
3,5 Millionen



Junge Erwachsene
(15-34)

Letzte 12 Monate
2,3 Millionen



MDMA



Erwachsene
(15-64)

Konsum:
Letzte 12 Monate
2,7 Millionen Lebenszeit
14,0 Millionen



Amphetamine



Erwachsene
(15-64)

Konsum:
Letzte 12 Monate
1,8 Millionen



Opioide



Hochrisiko-
Opioidkonsumenten
1,3 Millionen

Drogentherapienachfragen

Hauptdroge bei etwa
38 % aller Drogenthera-

Über

Bei 81
Überdosis
Opioid
63

Neue psychoaktive Substan



Konsum:

Letzte 12 Monate

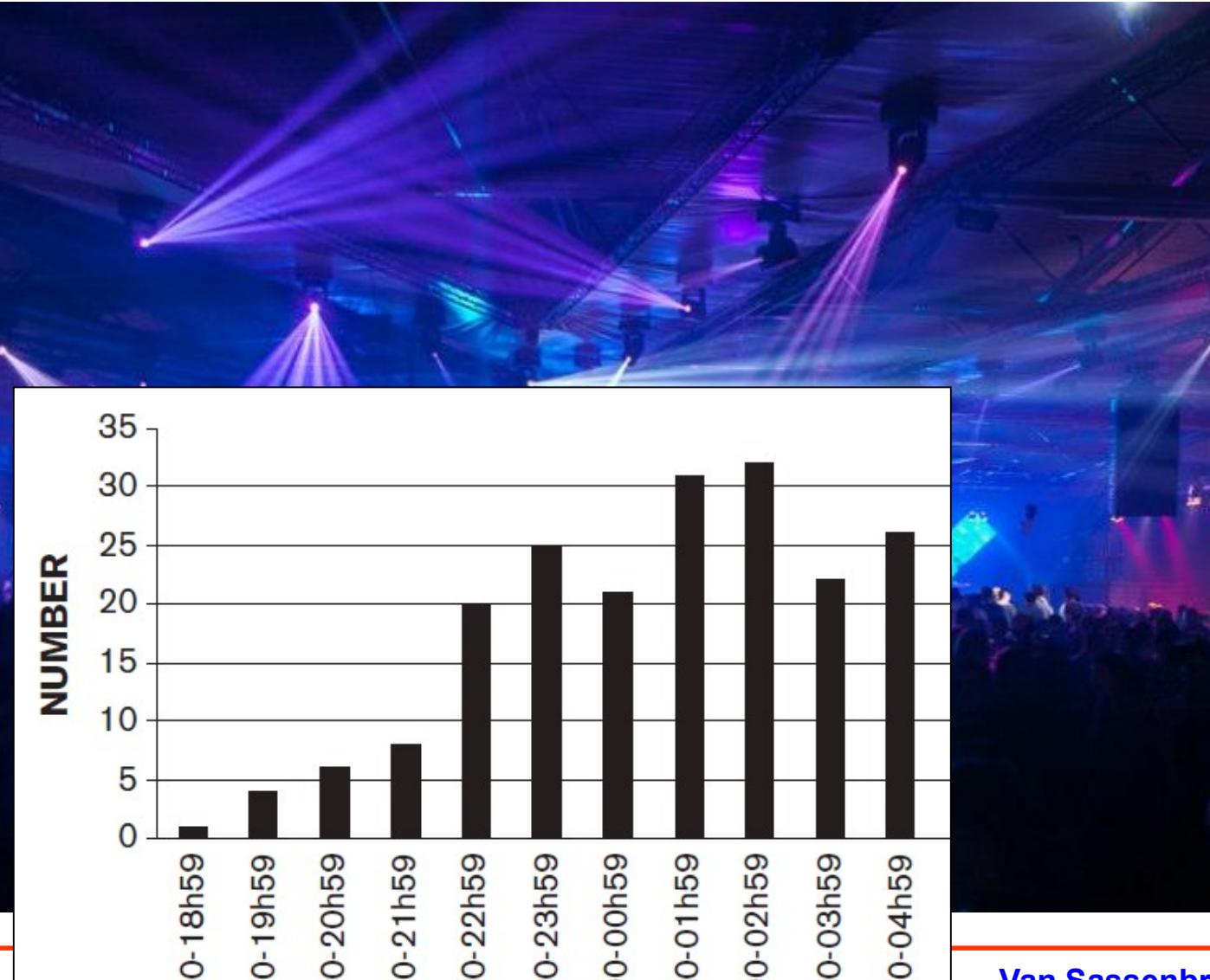


Lebenszeit



15- bis 16-jährige
Schüler
in 24 europäischen
Ländern

Medical Problems Related to Recreational Drug Use at Nocturnal Dance Parties



„I love techno“
37.000 Teilnehmer
„De Nacht“
12.000 Teilnehmer



Van Sassenbroeck-DK et al. Eur J Emerg Med 2003; 10: 30.

Medical Problems Related to Recreational Drug Use at Nocturnal Dance Parties

- **Medical problems in 65 -70 / 10.000 attendees**
- **Drug-associated medical problems in 15 / 10.000**
- **Particularly GHB and Ecstasy**
- „*Amnesty Box*“

2003 -> 2019 ?

Cannabis und Cannabinoide

Cannabis



Erwachsene
(15-64)

Konsum:
Letzte 12 Monate
23,5 Millionen **87,7 %**



Letzte 12 Monate
17,1 Millionen

Niedrigst

Cannabis:

- häufigste illegal konsumierte Droge in Europa
- Tetrahydrocannabinol (THC)
- Medizinisches Cannabis (analgetisch, antiemetisch, antidepressiv)

Synthetische Cannabinoide:

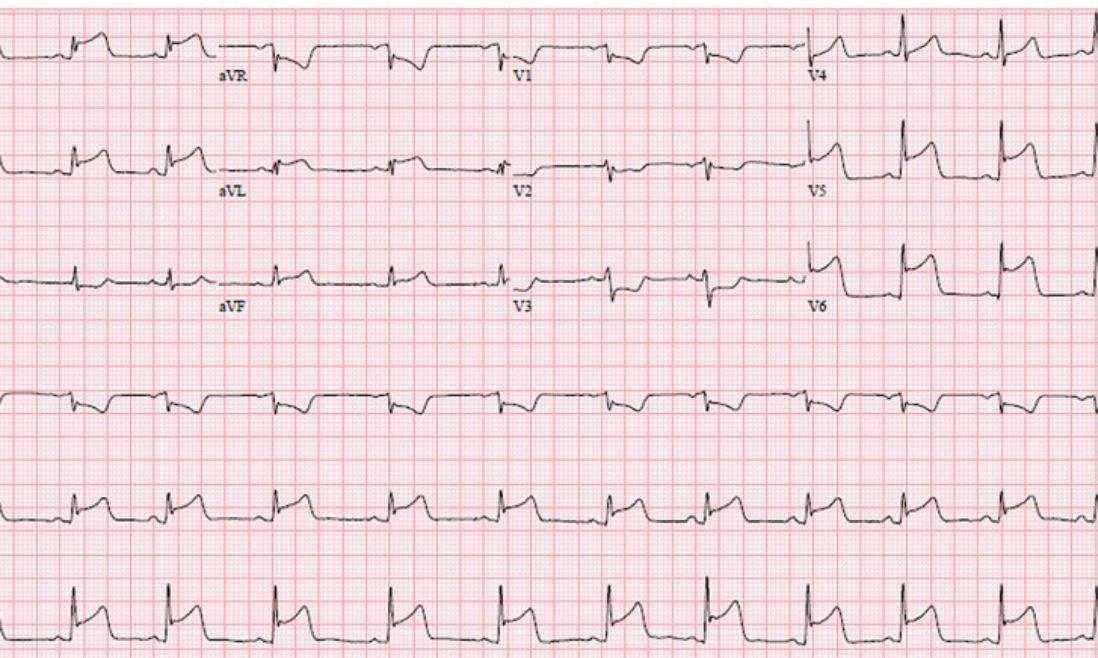
- illegale Herstellung
- in Räuchermischungen
- z.B. Spice
- aus dem Internet, aus Headshops
- große Gefahr seit einigen Jahren

Cannabis: Cardiovascular Effects

- Increased heart rate / tachycardia

Cannabinoids
Cannabimimetics

Marihuana-induced Myocarditis Syndrome



Kariyanna-PT et al. Am J Med Case Rep 2018; 6: 169-172

Marihuana-induced Type I Brugada Pattern



Kariyanna-PT et al. Am J Med Case Rep 2018; 6: 134-135

Singh-A et al. Cardiol Ther 2018; 7: 4

Synthetic Cannabinoids

Table 1. CB₁ receptor affinities (mean±SEM) of cannabimimetic indoles 5, 9–25, 27 and related compounds

Compd	<i>K_i</i> (nM)
Δ ⁹ -THC (1)	41±2 ^a
WIN-55,212-2 (3)	9.9±1.0 ^b
1-Pentyl-1 <i>H</i> -indol-3-yl-(1-naphthyl)methane (9, JWH-175)	22±2
1-Pentyl-1 <i>H</i> -indol-3-yl-(4-methyl-1-naphthyl)methane (10, JWH-184)	23±6
1-Pentyl-1 <i>H</i> -indol-3-yl-(4-methoxy-1-naphthyl)methane (11, JWH-185)	17±3
2-Methyl-1-pentyl-1 <i>H</i> -indol-3-yl-(1-naphthyl)methane (12, JWH-196)	151±18
2-Methyl-1-pentyl-1 <i>H</i> -indol-3-yl-(4-methyl-1-naphthyl)methane (13, JWH-194)	127±19
2-Methyl-1-pentyl-1 <i>H</i> -indol-3-yl-(4-methoxy-1-naphthyl)methane (14, JWH-197)	323±28
1-Penty	9±5 ^c
1-Penty	0.69±0.05
1-Penty	1.2±0.1 ^d
2-Meth	9.5±4.5 ^c
2-Meth	5.0±2.1
2-Meth	4.5±0.1 ^d
1-[2-(4-	113±28
1-[2-(4-	41±13
Morpholinomethyl-1 <i>H</i> -indol-3-yl-(4-methyl-1-naphthyl)methane (21, JWH-192)	20±2
1-[2-(4-	42±5
1-[2-(4-	6±1
1-[2-(4-	10±2
E-1-[1-	26±4
2-Ethyl	52±5



- Symptomatik nach Konsum der zahlreichen synthetischen Cannabinoide nicht vorhersehbar
- Praktisch alle Symptome möglich (Leber, Lunge, Herz, etc.)

Informationen in dieser Publikation:

- Strukturformeln einer Vielzahl von synthetischen Cannabinoiden
- Untersuchungen zur Bindungs-Affinität am CB₁-Rezeptor
- Informationen für „Profis“ derartig detailliert
- Nachsynthese problemlos möglich

^aRef 26

^bRinaldi

Soubrie

^cRef 15

^dRef 16

; Ferrara, P.;

Cocaine und „Crack“

Kokain



Erwachsene
(15-64)

Konsum:

Letzte 12 Monate Lebenszeit

3,5 Millionen 17,5 Millionen



Letzte 12 Monate

2,3 Millionen



- Starkes (psychisches) Suchtpotential
- Konsum deutlich steigend

Basic Risks:

Age, sex, race, diabetes, hypertension, heart failure, PAD, CVD, obesity/overweight, COPD, smoking, PCI, prior CABG

Risky Behaviors:

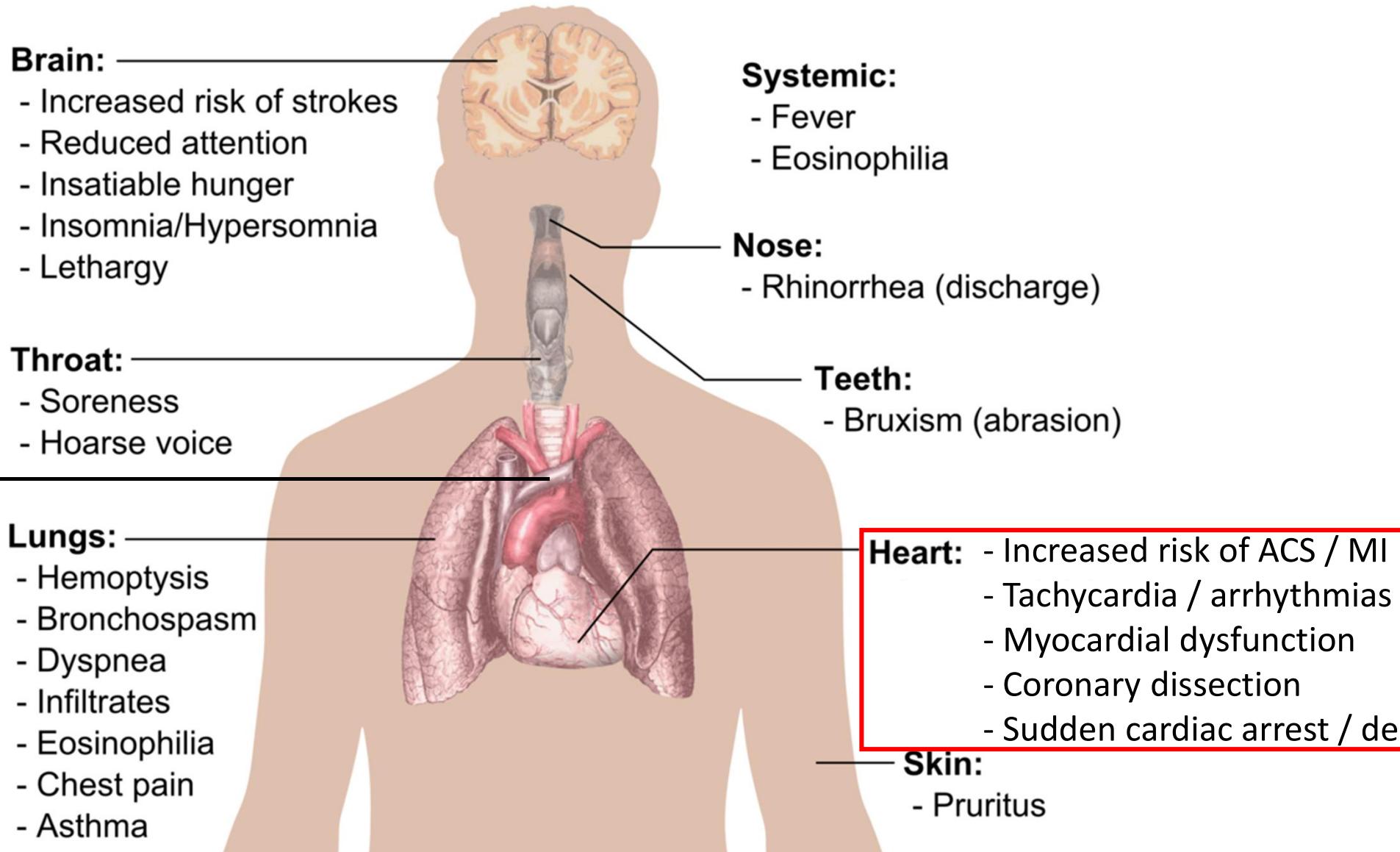
Other drug use, alcohol abuse, tobacco use

Cocaine Use

Causal Pathway :
CHF, cardiogenic shock

Physiological Effects of Cocaine: „Crack Whips the Heart“

blood vessels:
- Constriction
- Hypertension
- Dissection



Cardiovascular Consequences of Cocaine Use

Sympathetic nervous system

- Sympathomimetic effects
- Increased sensitivity to norepinephrine
- Inhibition of catecholamine reuptake
- Increased heart rate, blood pressure, contractility
- Increased myocardial oxygen demand

Cardiomyocytes

- Blockade of sodium and potassium channels depresses cardiovascular parameters
- Interference with calsequestrin-mediated calcium storage and release disrupts excitation-contraction coupling
- Progressive oxidative stress causes mitochondrial damage and cell death

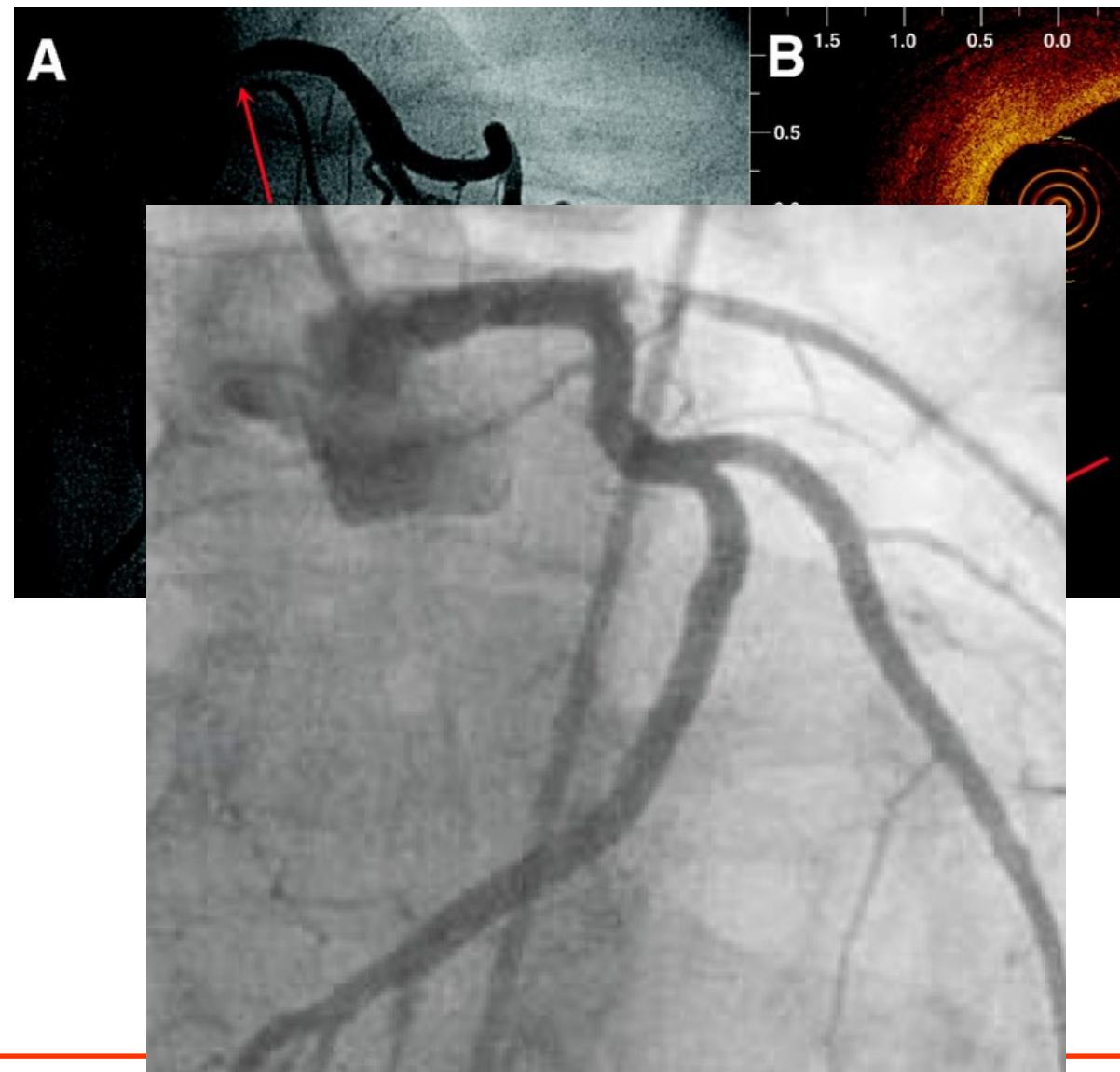
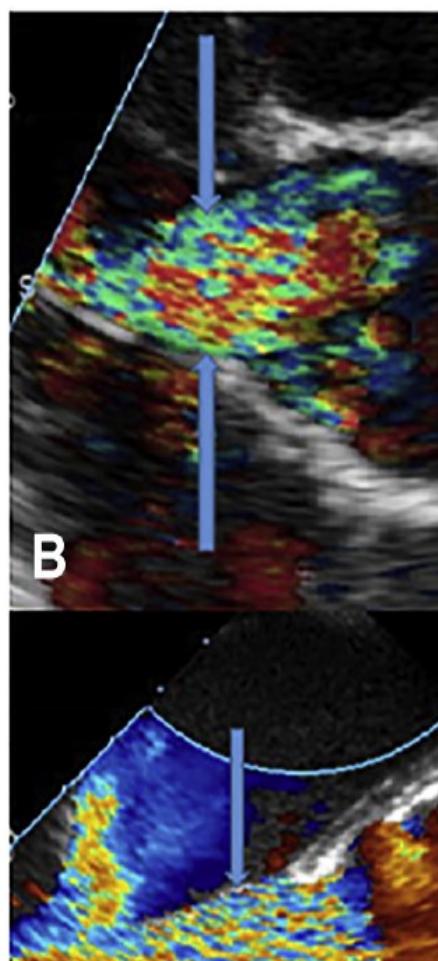
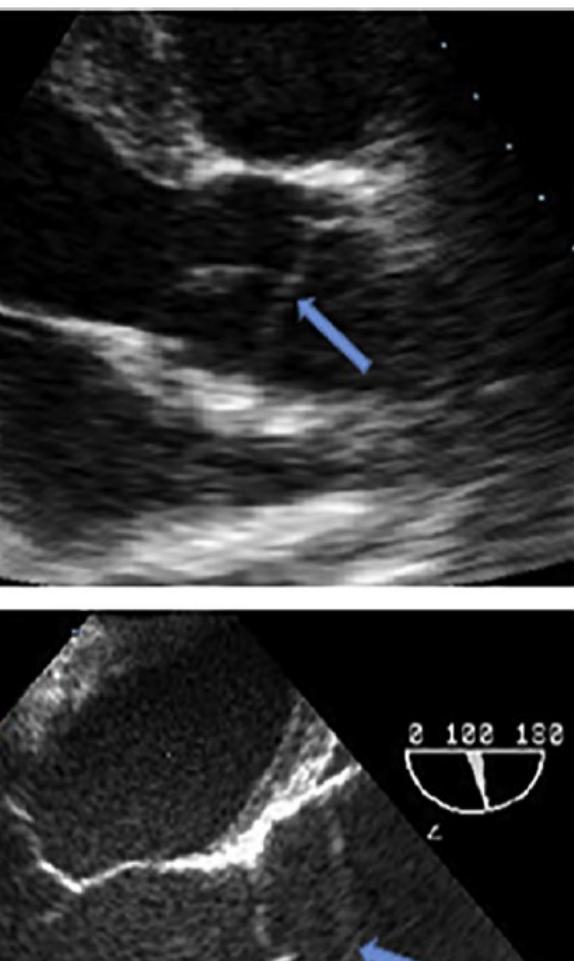
Va

- Vasoconstriction
- Prothrombotic state
- Increased platelet aggregation
- Endothelial dysfunction
- Thrombosis
- Decreased coronary blood supply

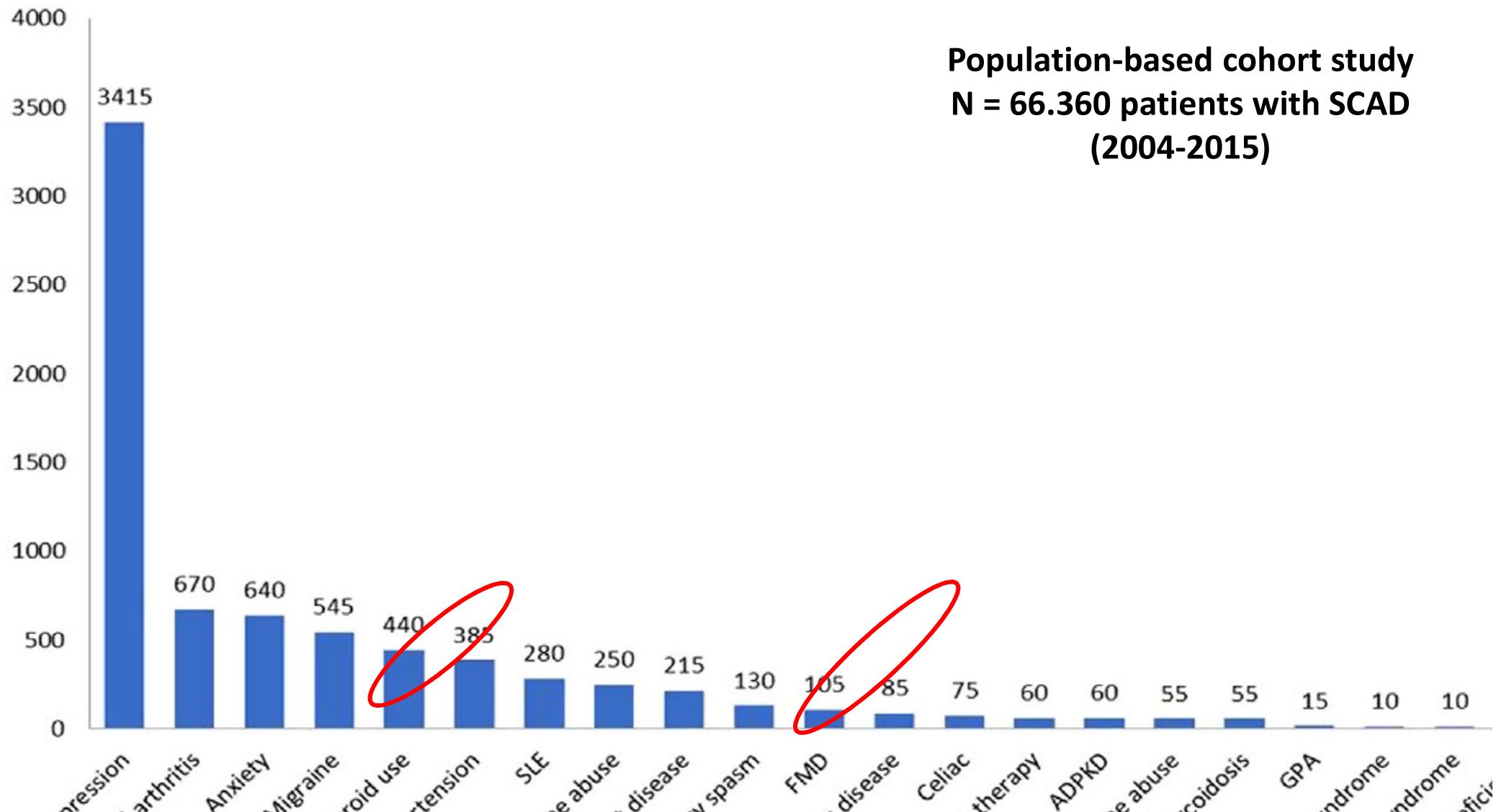
Short-term cardiovascular consequences

Long-term cardiovascular consequences

Cocaine-Associated Dissections of Aorta and Coronary Arteries



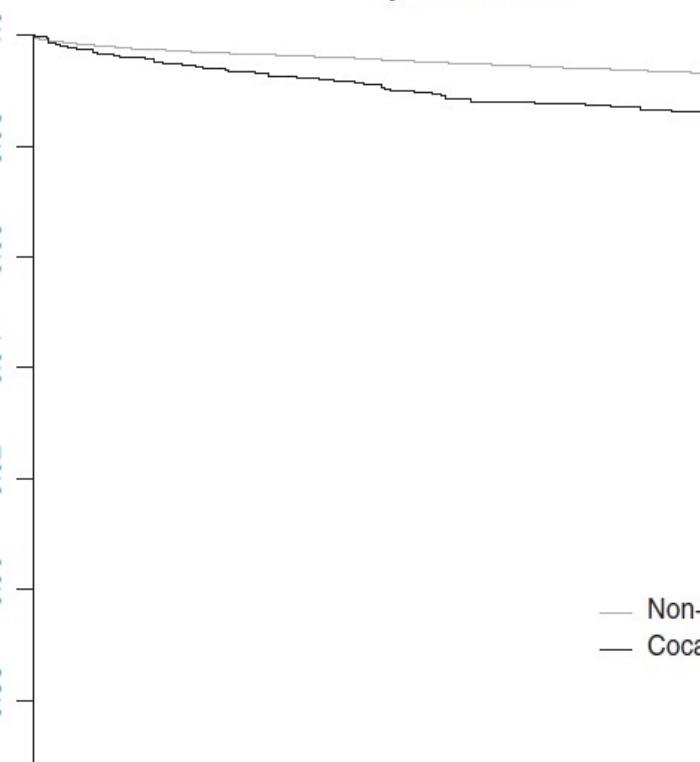
Conditions associated with Spontaneous Coronary Artery Dissect



CART: Cocaine Use and Cardiovascular Outcomes

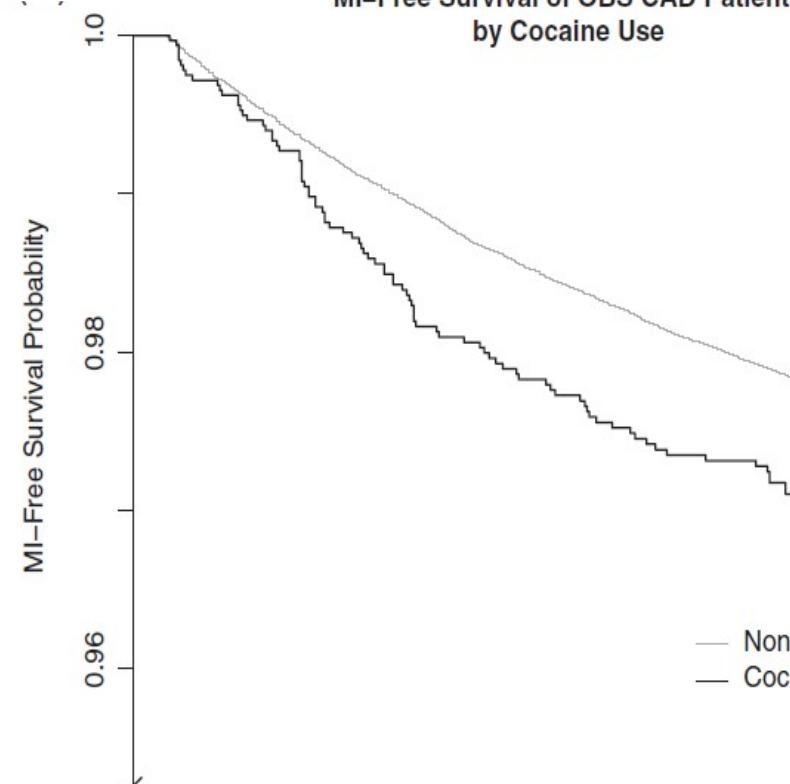
Survival

Survival of OBS CAD Patients by Cocaine Use



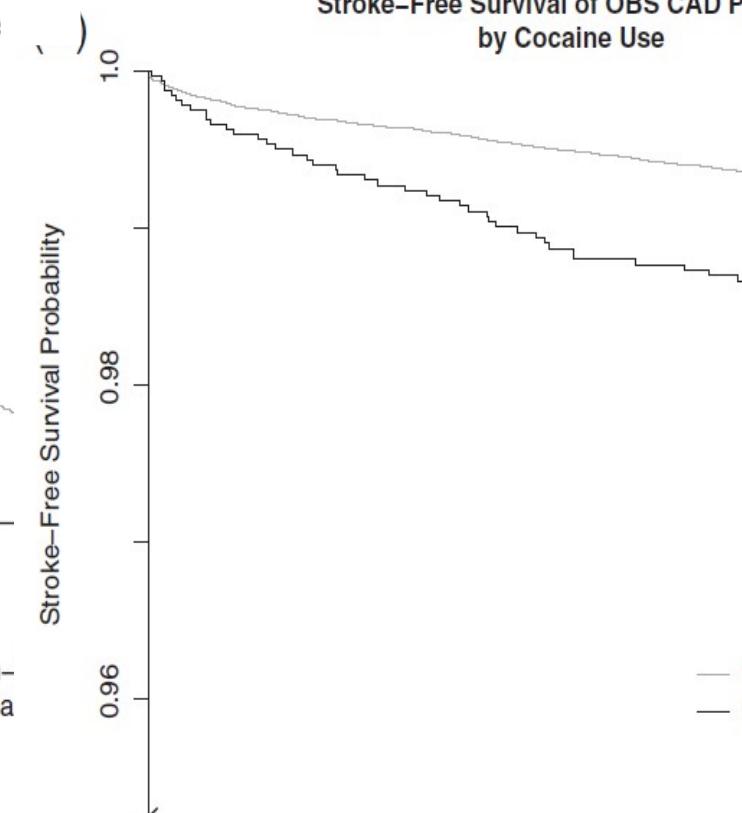
MI-free Survival

MI-Free Survival of OBS CAD Patient by Cocaine Use

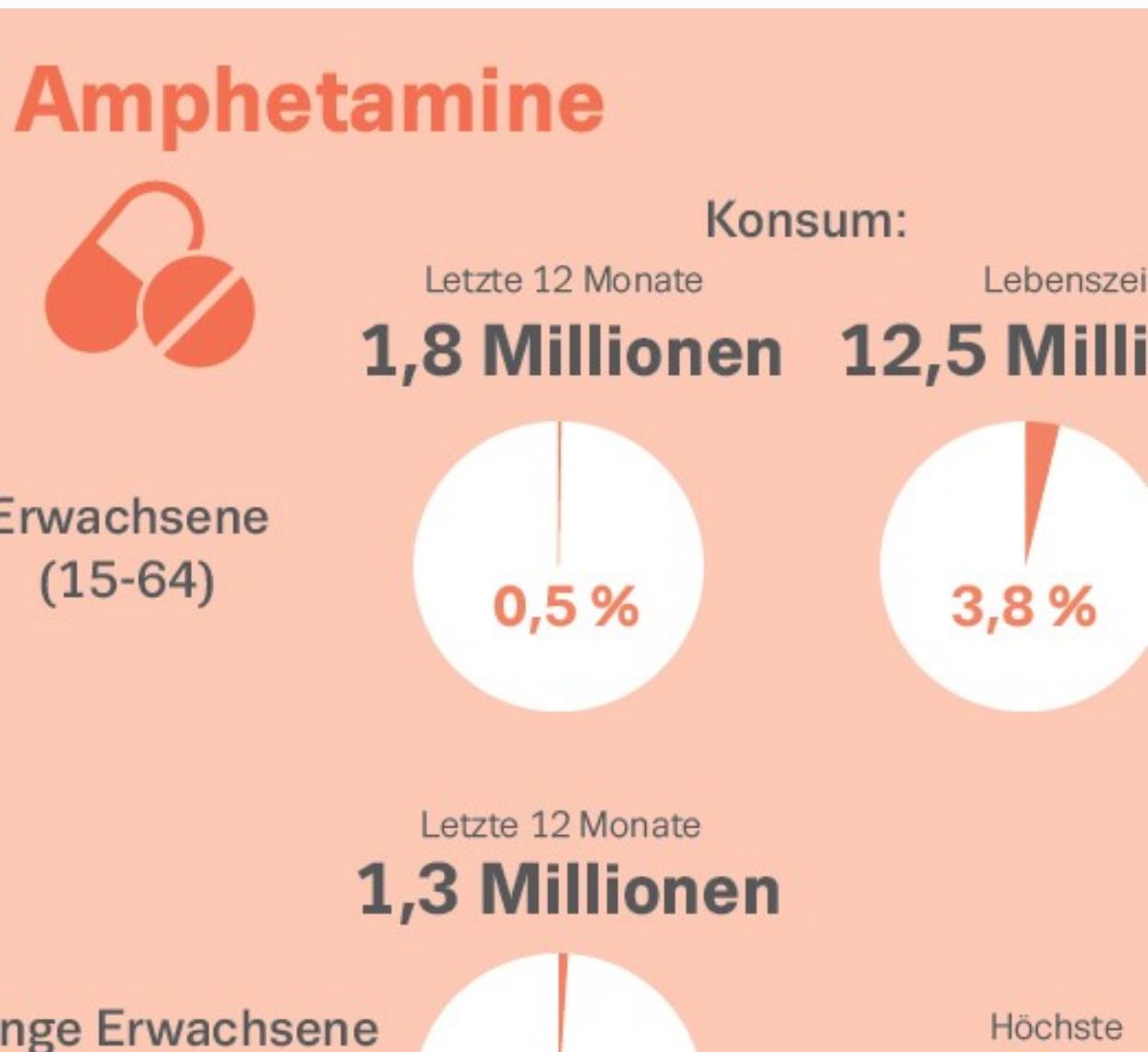


Stroke-free Survival

Stroke-Free Survival of OBS CAD P by Cocaine Use



Amphetamine / Methamphetamine



- Struktur Katecholamin-ähnlich
- Release von Noradrenalin und Dopamin

- Überstimulation des Sympathikus (indirektes Sympathomimetikum)

➤ **Amphetamin**

➤ **Methamphetamine (Crystal Meth)**

➤ **Ephedrin**

Kardiovaskuläre Effekte:

- Hypertonie
- Tachykardie
- VTs, Kammerflimmern
- Kardiomyopathie

MDMA / Ecstasy / Molly

MDMA



Erwachsene
(15-64)

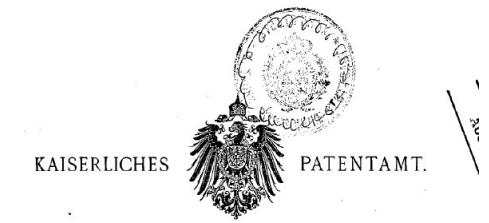
Konsum:
Letzte 12 Monate
2,7 Millionen **14,0 M**



Letzte 12 Monate
2,3 Millionen

Junge Erwachsene

- Gilt als Partydroge
- erstmals im Labor von E. Merck synthetisiert
- ZNS: Release von Serotonin und NA



PATENTSCHRIFT

— № 274350 —

KLASSE 12*q*. GRUPPE 32/*10*.

FIRMA E. MERCK IN DARMSTADT.

Verfahren zur Darstellung von Alkyloxyaryl-, Dialkyloxyaryl- und Alkylenedioxyarylpantanen bzw. deren am Stickstoff monoalkylierten Derivaten.

Patentiert im Deutschen Reiche vom 24. Dezember 1912 ab.

In der Literatur ist die Anlagerung zweier Atome Brom an Arylpropylene der allgemeinen Formeln: $R \cdot C H_2 \cdot C H : C H_2$ und $R \cdot C H : C H \cdot C H_3$, in welchen R einen ätherifizierten Arylgruppen:

5 (z. B. — $C_6H_4 \cdot OCH_3$ — $C_6H_5\overset{O}{\diagdown}CH_2$ — $C_6H_5\overset{O}{\diagup}CH_2$ — $C_6H_5\overset{O}{\diagdown}OCH_3$)

bedeutet, schon des öfteren beschrieben, dagegen ist die Anlagerung von Bromwasserstoffsäure an diese Doppelbindungen noch niemals durchgeführt worden. Es wurde nunmehr die unerwartete Beobachtung gemacht, daß Halogenwasserstoffsäuren unter 10 ungeeigneten Bedingungen sich an die erwähnten ungesättigten Verbindungen unter Bildung der bisher unbekannten Alkyloxy-, Dialkyloxy- oder Alkylenedioxyarylhalogenpropane anlagern,

Die Abkömmlinge des Propenylbenzo Anethol, Isosafrol, addieren Halogenstoff unter Bildung von α -substituierten (lieferten) n-Propylhalogeniden:

$C_6H_5 \cdot O \cdot C_6H_4 \cdot C H : C H \cdot C H_3 +$
 $= C_6H_5 \cdot O \cdot C_6H_4 \cdot C H (Br) \cdot C H_3$.

Die entstandenen Halogenwasserstoffsprodukte sind schwere, schwach i. Ole. Sie sind verhältnismäßig unb.

MA = 3,4-Methylendioxy-N-methylamphetamin

MDMA / Ecstasy / Molly



- „normales Ecstasy“
- Liquid Ecstasy (Champagne-like):
 - GHB (Gamma Hydroxybutyrate), Somsanit
 - GBL (Gammabutyrolacton)
 - 1,4 Butandiol
- Herbal Ecstasy - aus Ephedra

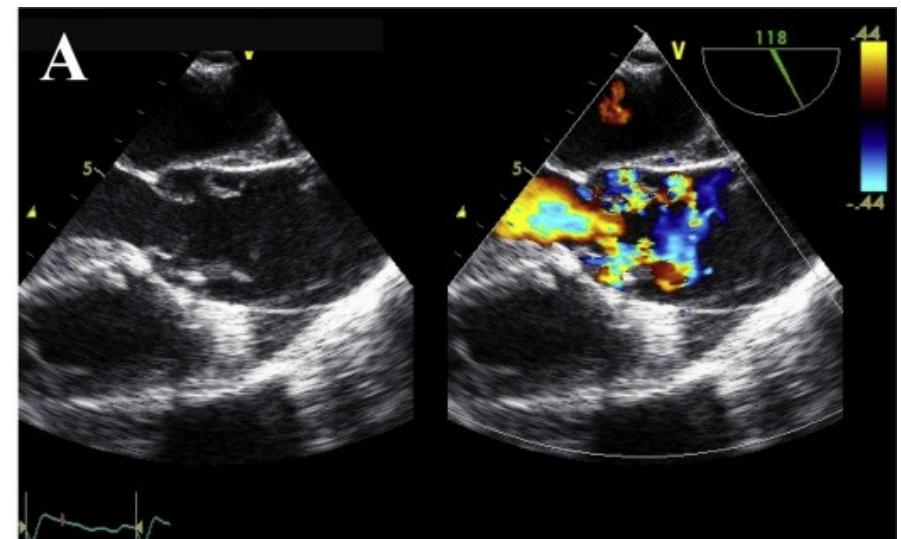


- Euphorie
- Empathie
- Tachykardie
- Hypertonie
- Hyperthermie

Acute ascending aortic dissection
MDMA/ecstasy use: A case report



Aortic Dissection After Ingestion of "Ecstasy" (MDMA)
Johan Duflou; Adam Mark



Opioide / synthetische Opioide

Opioide



Hochrisiko-
Opioidkonsumenten
1,3 Millionen

Drogentherapienachfragen

Hauptdroge bei etwa
38 % aller Drogenthera-

Bei 81
Überdosis
Opioiden
63%

- Opioid-Krise in USA
- Synthetische Opioide
- z.T. extrem potente Substanzen

ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 consecutive medical patients¹ who were monitored consecutively. Of these, there were 11,882 patients who received at least one narcotic analgesic. In this population, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. One case of addiction was considered major in only one instance. The other three cases of addiction were minor. The substances implicated were meperidine in two patients,² Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

J.

HERSHEL

Boston Collaborative

Surveillance

Waltham, MA 02154

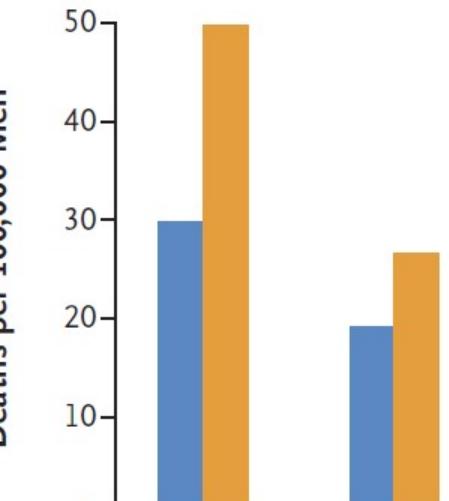
Boston University Medical Center

One short letter's huge impact on the opioid epidemic

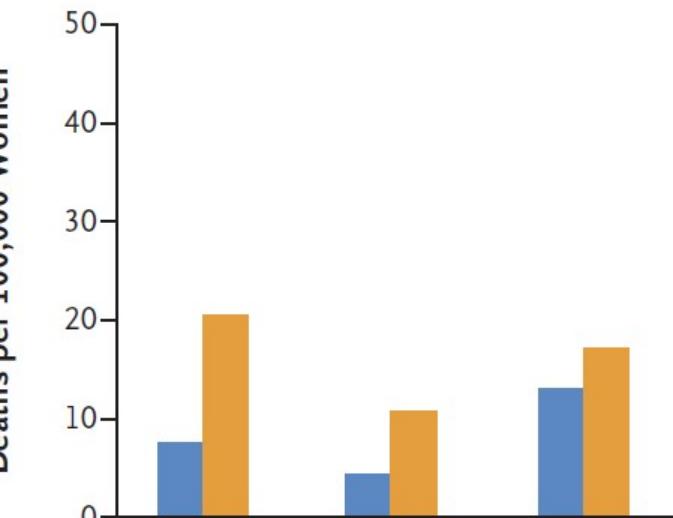
By Nadia Kounang, CNN

Opioid Use, Unintentional Overdose, and Suicide

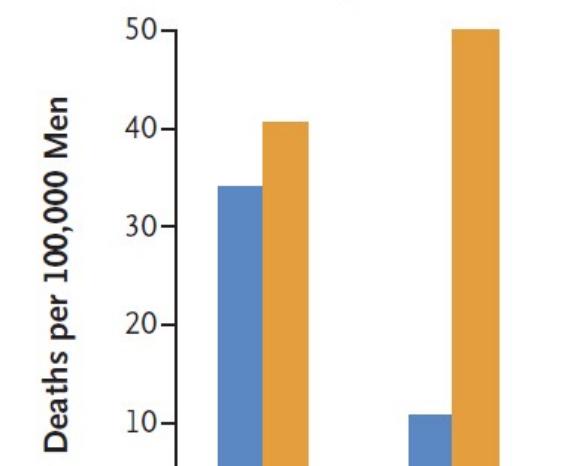
Men 18–40 Yr of Age



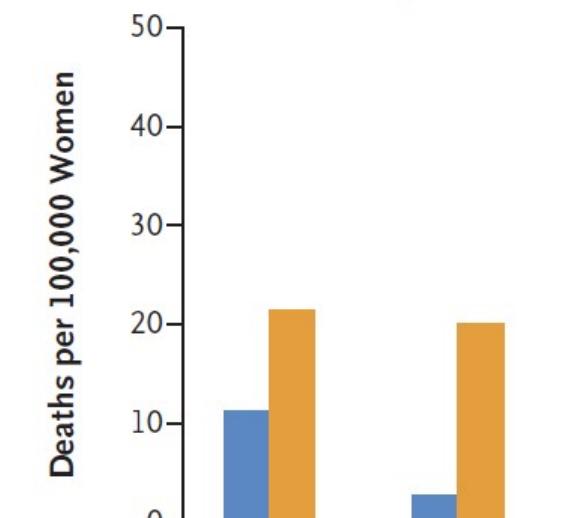
Women 18–40 Yr of Age



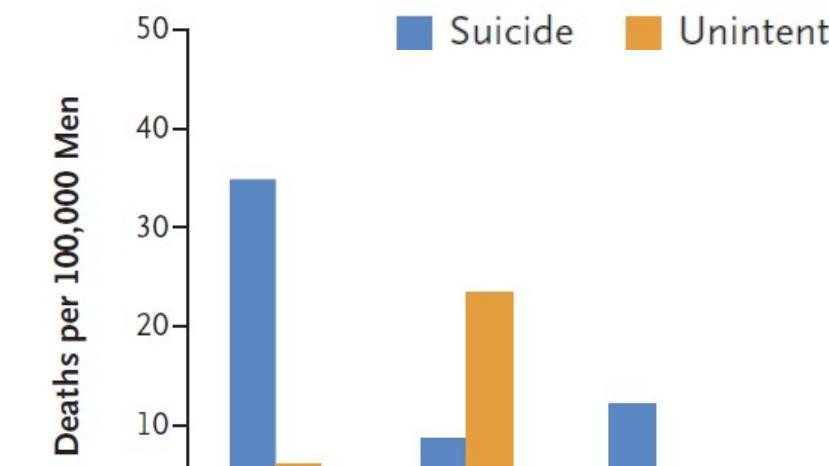
C Men 41–64 Yr of Age



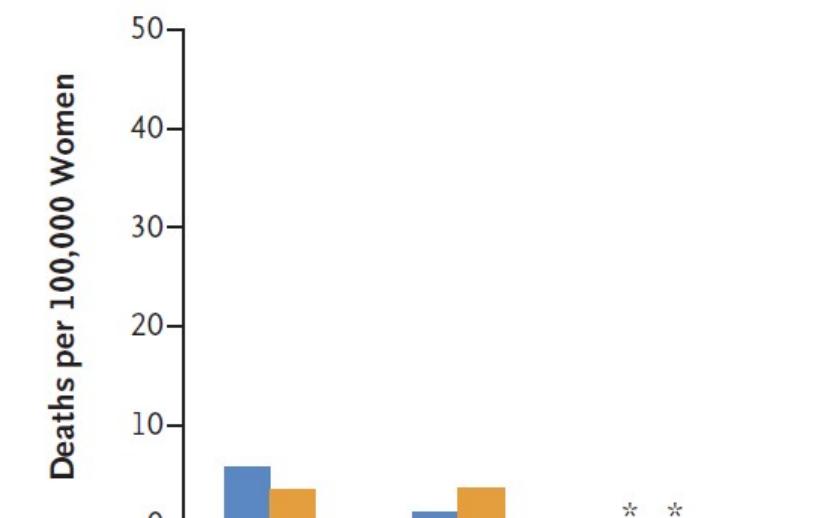
D Women 41–64 Yr of Age



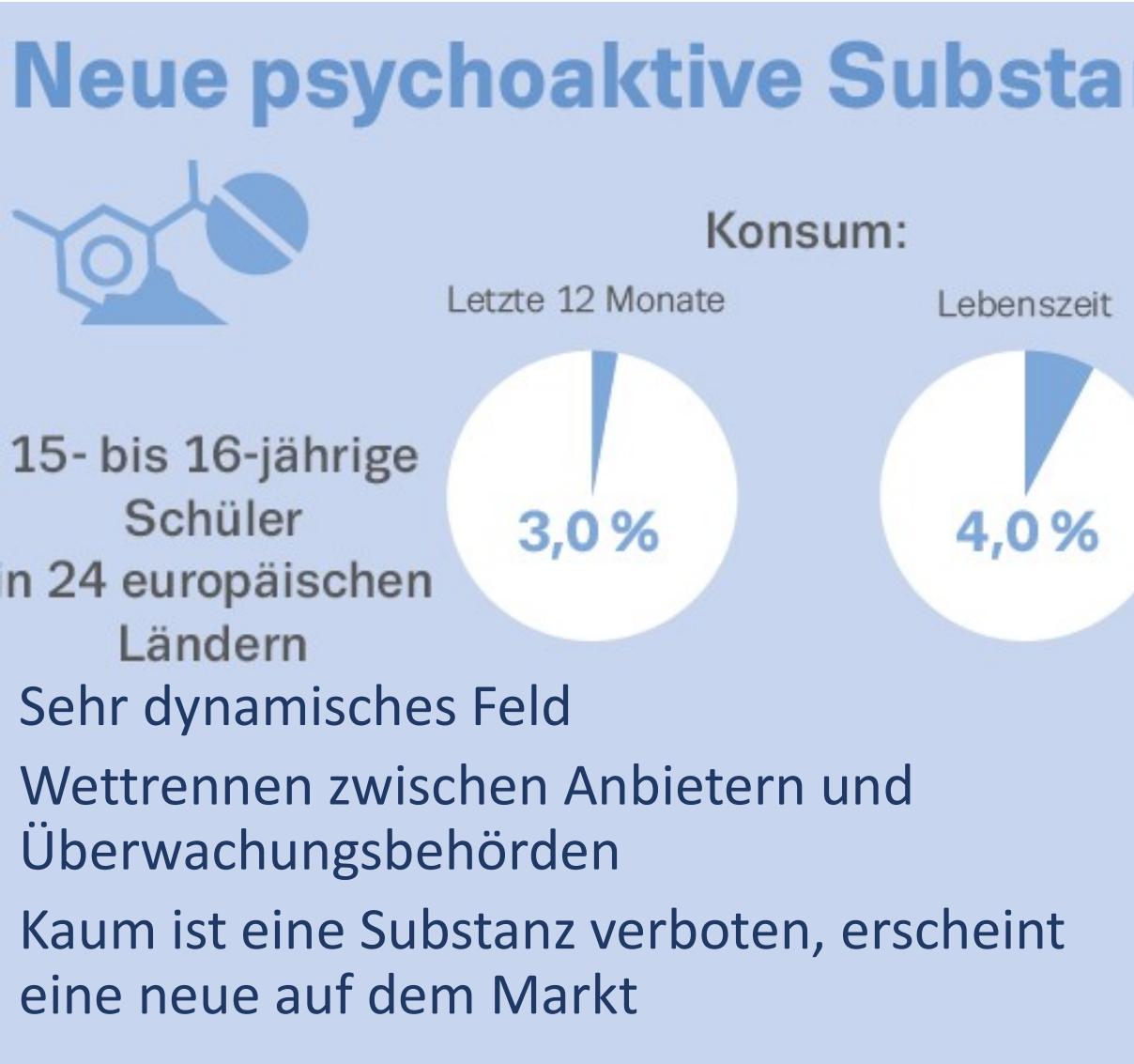
E Men ≥ 65 Yr of Age



F Women ≥ 65 Yr of Age



Neue psychoaktive Substanzen (NPS)



- Synthetische Cannabinoide
- Synthetische Opioide
- Synthetische Cathinone (MDPV
(Ursprung: Pflanze Khat aus dem Yemen))
- Benzodiazepine

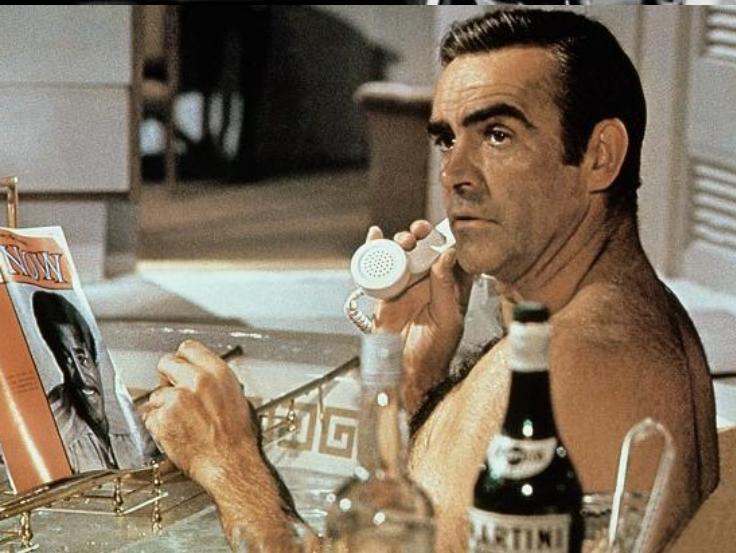
Neue Drogen:

- *Krokodil* aus Russland
 - *Desomorphin*
-
- Häufig sehr potente Substanzen
 - Sehr gefährlich
 - Unvorhersehbare Effekte auch zahlreiche Organsysteme inkl. Herz-/Kreislauf

Cardiovascular Effects of Modern Lifestyle Drugs

	Arrhythmias Tachycardia	Dissections (coronary / aortic)	Hypertension	Vasoconstriction Vasospasm	Myocardial infarction	Heart Failure	Cardiac arrest , SD
cannabis / nabnoids	+	-	-	+	+	-	+
caine / “back”	+	+	+	+	+	+	+
MA / Ecstasy	+	+	+	-	+	+	+
phetamins / orthamphetamins	+	+	+	-	+	+	+
oids / thetic opioids	+	+	-	-	-	-	-
v psychoactive gs (NPS)	+	+	+	+	+	+	+

Licence to swill: James Bond's drinking decades



*.....shaken,
not stirred....*

Licence to swill: James Bond's drinking across decades



1 Drinking by James Bond and other characters in his films, by decade

	Events	1960s	1970s	1980s	1990s	2000s
Number of movies	—	6	5	5	3	3
Total movie time (hours)	—	12.0	10.3	10.9	6.3	6.0
Number of drinking events by Bond	—	29	15	23	10	2
Drinking by Bond (per movie), mean						
Alcohol use events	109	4.8	3.0	4.6	3.3	7.0
Time from movie start to first drink (minutes)	—	24.7	17.8	20.4	27.0	22.0
Drink was cocktail or spirits	59 [†]	3.2	1.2	1.6	2.0	4.0
Drink was martini (cocktail group subset)	18	0.7	0.6	0.6	0.7	1.0
Drink was champagne or other wine	45 [†]	1.5	1.8	3.0	1.3	2.0
Smokes while drinking	6	0.3	0.2	0.2	0.0	0.0
Drinking by women (per movie), mean						
Alcohol use events, lead women [‡]	37	1.2	1.4	1.8	0.7	2.0
Alcohol use events, Bond's sexual partners [§]	17	0.5	0.4	0.8	1.0	0.0
Other (per movie), mean						
Alcohol mentioned outside of Bond's drinking	51	1.3	2.2	2.0	2.0	2.0

Licence to swill: James Bond's drinking decades



Results: Bond has drunk heavily and consistently for decades (109 drinking events; mean 4.5 events per decade). Chronic risks for Bond include frequent driving vehicles (including in chases) prior to fights, gambling, operating complex machinery or devices around dangerous animals, extreme athletic performance, and sex.

Conclusions: James Bond has a severe chronic alcohol problem. He should consider seeking professional help and developing strategies for managing on-the-job stress.

The image shows two young cannabis plants with green leaves against a plain white background. The plant on the left is more prominent, showing a central stem with several large, serrated leaves. The plant on the right is slightly smaller and positioned lower in the frame.

Vielen Dank!